

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A modified antibody of class IgG with FcRn binding affinity altered relative to that of an unmodified antibody, said modified antibody comprising a heavy chain variable region and a heavy chain constant region wherein said heavy chain constant region comprises glutamic acid or glutamine at least amino acid residue 250, EU numbering, is glutamic acid or glutamine and leucine or phenylalanine at amino acid residue 428, EU numbering, is leucine or phenylalanine.

2. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.

3. (Original) The modified antibody according to Claim 1, wherein said unmodified class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.

4. (Canceled)

5. (Previously presented) The modified antibody according to Claim 2, wherein said unmodified class IgG antibody is a human class IgG1 antibody.

6. (Previously presented) The modified antibody according to Claim 1, wherein the unmodified antibody is

OST577-IgG2M3, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOS: 1, 2, 4, and 5, respectively, or

OST577-IgG1, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOs: 1, 3, 4, and 5, respectively.

7. (Cancelled)

8. (Previously presented) A modified antibody of class IgG with FcR<sub>n</sub> binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain constant region wherein

amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid or glutamine.

9. (Previously presented) The modified antibody according to Claim 1, wherein amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine.

10. (Previously presented) The modified antibody according to Claim 1, wherein amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

11. (Previously presented) A modified antibody of class IgG with FcR<sub>n</sub> binding affinity altered relative to that of an unmodified antibody, comprising a heavy chain constant region wherein:

(a) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

12. (Previously presented) The modified antibody according to Claim 1, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

13-14. (Canceled)

15. (Previously presented) The modified antibody according to Claim 8, wherein said class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.

16. (Previously presented) The modified antibody according to Claim 8, wherein said class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.

17. (Previously presented) The modified antibody according to Claim 15, wherein said unmodified class IgG antibody is a human class IgG1 antibody.

18. (Original) The modified antibody according to Claim 1, wherein the modified antibody has a higher binding affinity for FcRn at pH 6.0 than at pH 7.4.

19. (Currently Amended) An antibody comprising a heavy chain variable region and a heavy chain constant region substantially identical to that of a naturally occurring class IgG antibody, except for wherein at least the heavy chain constant region comprising glutamic acid or glutamine at amino acid residue 250, EU numbering, is glutamic acid or glutamine and leucine or phenylalanine at amino acid residue 428, EU numbering, is leucine or phenylalanine; and wherein the *in vivo* serum half-life of said antibody is increased relative to the naturally occurring antibody.

20. (Original) The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.

21. (Original) The antibody according to Claim 19, wherein said naturally occurring class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.

22. (Canceled)

23. (Previously presented) The antibody according to Claim 20 wherein said naturally occurring class IgG antibody is a human class IgG1 antibody.

24. (Currently amended) An antibody comprising a constant region substantially identical to that of a naturally occurring class IgG antibody, except for wherein amino acid residue 250, EU numbering, from the heavy chain constant region being [[is]] glutamic acid or glutamine.

25. (Previously presented) The antibody according to Claim 19, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine.

26. (Previously presented) The antibody according to Claim 19, wherein said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

27. (Currently amended) An antibody comprising a constant region substantially identical to that of a naturally occurring class IgG antibody, except for wherein:

(a) amino acid residue 250, EU numbering, from the heavy chain constant region being [[is]] glutamic acid and said amino acid residue 428, EU numbering, from the heavy chain constant region being [[is]] phenylalanine;

(b) amino acid residue 250, EU numbering, from the heavy chain constant region being [[is]] glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region being [[is]] phenylalanine; or

(c) amino acid residue 250, EU numbering, from the heavy chain constant region being [[is]] glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region being [[is]] leucine; and

wherein the *in vivo* serum half-life of said antibody is increased relative to the naturally occurring antibody.

28. (Previously presented) The antibody according to Claim 19, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

29-30. (Canceled)

31. (Previously presented) The antibody according to Claim 24, wherein said class IgG antibody comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.

32. (Previously presented) The antibody according to Claim 24, wherein said class IgG antibody comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.

33. (Previously presented) The antibody according to Claim 31, wherein said unmodified class IgG antibody is a human class IgG1 antibody.

34. (Previously presented) A modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, with an *in vivo* mean elimination half-life at least about 1.8-fold longer than that of the corresponding unmodified class IgG antibody and

wherein in said heavy chain constant region, residue 250, EU numbering, is glutamic acid or glutamine and residue 428, EU numbering, is leucine or phenylalanine.

35. (canceled)

36. (Previously presented) A modified antibody of class IgG with an *in vivo* mean elimination half-life at least about 1.8-fold longer than that of the corresponding unmodified class IgG antibody, wherein:

- (a) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;
- (b) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or
- (c) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

37. (Previously presented) The modified antibody of Claim 34, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

38. (canceled)

39. (Previously presented) A modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, with an *in vivo* mean serum clearance rate at least about 1.8-fold lower than that of the corresponding unmodified class IgG antibody and

wherein in said heavy chain constant region, residue 250, EU numbering, is glutamic acid or glutamine and residue 428, EU numbering, is leucine or phenylalanine.

40. (canceled)

41. (Previously presented) A modified antibody of class IgG with an *in vivo* mean serum clearance rate at least about 1.8-fold lower than that of the corresponding unmodified class IgG antibody wherein

(a) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine;

(b) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is phenylalanine; or

(c) amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

42. (Previously presented) The modified antibody of Claim 39, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is leucine.

43-51. (Canceled)

52. (Previously presented) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the modified antibody according to Claim 1.

53. (Currently amended) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the antibody having a constant region substantially identical to that of a naturally occurring class IgG antibody according to Claim 20.

54-56. (Canceled)

57. (Currently amended) A method for preparing the [[an]] antibody of Claim 1, said method comprising substituting residues 250 and 428, EU numbering, in the heavy chain constant region with glutamic acid or glutamine at residue 250 and leucine or phenylalanine at residue 428.

58 (Previously presented) A method of producing a modified antibody of class IgG, and comprising a heavy chain variable region and a heavy chain constant region, with

an altered binding affinity for FcRn and/or an altered serum half-life as compared with the unmodified antibody, said method comprising:

- (a) preparing an expression vector comprising a suitable promoter operably linked to DNA encoding at least a variable region and a constant region of an immunoglobulin heavy chain in which residue 250, EU numbering, is substituted with glutamic acid or glutamine and residue 428, EU numbering, is substituted with leucine or phenylalanine;
- (b) transforming host cells with said vector; and
- (c) culturing said transformed host cells to produce said modified antibody.

59. (Original) The method according to Claim 58, further comprising: preparing a second expression vector comprising a promoter operably linked to DNA encoding a complementary immunoglobulin light chain and further transforming said host cells with said second expression vector.

60. (canceled)

61. (Previously presented) The method according to Claim 58, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine.

62. (Previously presented) The method according to Claim 58, wherein said amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with leucine.

63. (Previously presented) The method according to Claim 58, wherein

- (a) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamic acid and amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with phenylalanine;

(b) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with phenylalanine; or

(c) said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine and amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with leucine.

64. (Previously presented) The method according to Claim 58, wherein said amino acid residue 250, EU numbering, from the heavy chain constant region is substituted with glutamine and said amino acid residue 428, EU numbering, from the heavy chain constant region is substituted with leucine.

65-66. (Canceled)

67. (Previously presented) The method according to Claim 58, wherein said antibody of class IgG comprises a heavy chain constant region of a human IgG1, IgG2, IgG2M3, IgG3 or IgG4 molecule.

68. (Previously presented) The method according to Claim 58, wherein said antibody of class IgG comprises a heavy chain constant region of a human IgG1 or IgG2M3 molecule.

69. (Previously presented) The method according to Claim 67, wherein said antibody of class IgG is a human class IgG1 antibody.

70. (Previously presented) The modified antibody according to Claim 8, wherein the unmodified antibody is

OST577-IgG2M3, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOS: 1, 2, 4, and 5, respectively, or

OST577-IgG1, with a heavy chain variable region, a heavy chain constant region, a light chain variable region, and a light chain constant region represented by SEQ ID NOs: 1, 3, 4, and 5, respectively.

71. (Previously presented) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the modified antibody according to Claim 8.

72. (Currently amended) An antibody fragment comprising a heavy chain constant region or a heavy chain Fc region of the antibody having a constant region substantially identical to that of a naturally occurring class IgG antibody according to Claim 15.

73. (Previously presented) The modified antibody according to Claim 8, wherein residue 250, EU numbering, from the heavy chain constant region is glutamic acid.

74. (Previously presented) The modified antibody according to Claim 8, wherein residue 250, EU numbering, from the heavy chain constant region is glutamine.

75. (Previously presented) A method for preparing an antibody of Claim 8, said method comprising substituting residue 250, EU numbering, in the heavy chain constant region with glutamic acid or glutamine.